

Sub C1  
11. (Amended) A method for detecting a functional mutation in a target up-stream regulatory gene comprising:

preparing a reference sample from reference cells having a wild-type up-stream regulatory gene corresponding to said target up-stream regulatory gene;

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preparing a target sample from target cells suspected of having a mutation in said target up-stream regulatory gene, said target cells being otherwise substantially similar to said reference cells;

detecting the expression of a plurality of more than 5 down-stream genes in said reference sample to obtain a reference expression pattern, said down-stream genes being up or down regulated by said wild-type up-stream regulatory gene;

detecting the expression of said plurality of down-stream genes in said target sample to obtain a target expression pattern; and

comparing said reference expression pattern with said target expression pattern to detect functional mutation in or inactivation of said target gene.

16. (Amended) The method of claim 11 further comprising the step of:

indicating a loss of wild-type function in said target gene if a significant number of said down regulated genes are expressed higher in said target sample than in said reference sample or if a significant number of said up-regulated genes are expressed lower in said target sample than in said reference sample.

17. (Amended) The method of claim 11 further comprising the step of:

indicating a gain of function mutation in said target gene if a significant portion of said down regulated genes are expressed lower in said target sample than in said reference sample or if a significant portion of said up-regulated genes are expressed higher in said target sample than in said reference sample.

Sub C2 29. (Amended) A method for detecting a p53 gene functional mutation in target cells comprising the steps of:

AIH preparing a reference sample from reference cells having a wild-type p53 gene, said reference cells being otherwise substantially similar to said target cells;

detecting the expression of a plurality of more than five down-stream genes in said reference cells and said target cells to obtain a target expression pattern and a reference expression pattern, said down-stream genes being up- or down-regulated by said wild-type p53 gene; and

comparing said reference expression pattern with said target expression pattern to detect said p53 functional mutation.

Sub C3 34. (Amended) An in-cell functional assay for a p53 sequence alteration comprising the steps of:

AI2 preparing a target sample from target cells having said p53 sequence alteration;

preparing a reference sample from reference cells having a wild-type p53 gene, said reference cells being otherwise substantially similar to said target cells;

detecting the expression of a plurality of more than 5 down-stream genes in said reference cells to obtain a reference expression pattern and in said target cells to obtain a target expression pattern, said down-stream genes being selected from the group consisting of p53 up-regulated genes and p53 down-regulated genes; and

comparing said reference expression pattern with said target expression pattern to determine the function of said p53 sequence alteration.